Methadone Maintenance for Opiate Dependence

JOHN C. KRAMER, M.D., *Irvine*

● *The use of the synthetic opiate methadone on a continuing maintenance scheduled is unquestionably the most successful and most widely applicable treatment for the control of opiate dependence. Though the medical aspects of the treatment are simple, the nature of the medication and the nature of the problems of opiate dependence are such that administration of a program requires careful attention. Because the problem is so serious both to society and the addict, it is urgent that we develop an adequate number of well run methadone programs throughout the state and the nation.*

OPIATE DEPENDENCE is a serious, chronic condition which threatens the lives and the health and the freedom of its victims. It leads almost inevitably to repeated episodes of institutionalization and concurrent illness. It destroys the families of the addicts as well as the addicts themselves. Apart from the personal tragedy wrought by addiction, it has serious consequences to society. As of December 31, 1966, 28.1 percent of the inmates in institutions under the authority of the California Department of Corrections were addicts.[1,2] To support their "habit," the majority must sell drugs or engage in other illicit enterprises. We in California spend tens of millions of dollars in apprehending, trying and incarcerating tens of thousands of addicts. The costs in theft and other crime against property may be even greater than the amounts we voluntarily appropriate.

From the Department of Psychiatry and Human Behavior, and Department of Medical Pharmacology and Therapeutics, University of California, Irvine, California College of Medicine.

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Reprint requests to: Orange County Medical Center, 101 South Manchester Avenue, Orange, Ca. 92668 (Dr. J.C. Kramer).

During the last ten years, a number of new approaches to the treatment of addicts have been tried, including Synanon, Daytop and similar programs, and civil commitment.[3] Though each has received enthusiastic support from its advocates and each boasts of succesfully rehabilitated addicts, none holds so much promise for so many as does methadone maintenance.

Methadone maintenance has been reported to be highly successful in controlling the addiction process.[4] By "the addiction process," I mean more than merely the pharmacological dependence on opiates but also the physical, psychological and social consequences of illegal opiate use. On the street, narcotics are generally taken intravenously. Hypodermic equipment is unsterile and drugs are impure; infection, both bacterial and viral is common; overdose and toxic reaction also is frequent; and nutrition and other health needs are neglected. In his search for narcotics and the money to buy them, the addict lives from hour to hour fulfilling or anticipating his needs for his next fix, with only the brief respite of the

intermittent heroin high. There is little time for family, friends or work. Though many addicts do have real concern for their families, their own oppressing needs are so profound that everything else suffers. Even when abstinence is achieved occasionally, the persistent desire for the drug effect remains.

A patient maintained on methadone in a supervised program, though physically dependent on this drug, is not subject to the other elements of the addiction process. His craving for opiates is suppressed, he is off the rollercoaster of highs and lows of several daily injections of narcotics, he has no need to engage in illegal activities, and he has time to devote to the ordinary activities of living. And despite the pessimistic view of what has been called "the addict personality," the overwhelming majority of methadone patients have, in fact, completely restructured their lives for the better.

Methadone is a synthetic opiate which has been used as an analgesic for 30 years. And in six years of experience with methadone maintenance, though fatal overdose is possible, no other serious toxic effect has been shown. A prediction was made about four years ago that regular use of methadone would probably produce personality deterioration and social demoralization.[5] The opposite has occurred. Few human manipulations have been devised which have improved the personality and the morals of so many people so rapidly.

The physician's morality in prescribing a narcotic for maintenance has also been challenged, but the legitimacy of providing insulin for diabetics, antipsychotic agents for schizophrenics, antiseizure medication for epileptics and a variety of other medicaments to other chronically ill people is not questioned on moral grounds. If a specific treatment produces substantial benefits to a patient with proportionately little to contraindicate it, it is logically accepted as a desirable treatment until something better comes along.

Methadone maintenance is intended for patients with a substantial and persistent history of dependence on opiates. Though variations of the treatment are being examined, most programs follow the general principles laid down by Dole and Nyswander.[4,6,7] The treatment proceeds in two phases: First the induction phase, and second, the continued treatment phase. During the induction phase, the patient is started on a moderate dose which over several weeks is increased to the final maintenance dose. Initial doses generally range from 10 to 40 mg a day, depending on the current level of tolerance of the patient, and the final dose generally ranges from 70 to 150 mg a day. Usually, the medication is given in a single daily dose of a dilute solution for oral ingestion.

During the induction phase, as the average daily dose is raised and for a few weeks thereafter, the patient may experience some mild discomfort which may include such symptoms as tiredness, blurred vision, diminished sexual interest, constipation, uticarial rash, and increased sweating. After the final dose has been reached, these side effects disappear with the exception of the constipation and the increased sweating. Some adjustment of the maintenance dose may be necessary but the adjustment is as frequently a decrease as an increase. Even during the induction phase, the side effects mentioned are not prominent and do not occur in all patients.

Pharmacologically, this treatment serves two purposes: At a dose of about 40 mg a day the craving for opiates disappears; second, at a dose of about 80 mg a day a "blockading" effect becomes prominent. Here some explanation is necessary. Although addicts who have been abstinent from opiates for long periods no longer suffer from withdrawal symptoms and do not have physical dependence upon it, they experience a persistent craving for the drug effect. Patients on methadone maintenance also feel normal, but, unlike the abstinent addicts, they have no sense of craving for heroin. Beyond the suppression of drug hunger, the effect previously mentioned, called "narcotic blockade," occurs. It is a result of the cross tolerance between methadone and other opiates. A patient on a blockading dose of methadone will experience little, or more often no, effect from use of additional opiates, even in rather large doses. Because of the slow metabolism of methadone, this blockading effect persists even should one daily dose be missed.[9] Though their drug hunger is suppressed, some patients during their early months on the program try heroin once or a few times to test if indeed a blockade truly exists. When they determine that it does, they almost invariably experiment no further.

Methadone is an interesting drug in other ways.

It is much less likely than other opiates to produce euphoria or sedation,[6] and tolerance is rapidly developed even for the small potential for these effects. Perhaps most significant is its unusually slow metabolism. Because of this, a single daily oral dose in a tolerant individual produces no important subjective effect, nor does the patient notice any changes between daily doses. Should a methadone patient skip a daily dose, he will notice, perhaps 36 or 48 hours after his last dose, some muscular aching and some nasal congestion. Unless he is aware that he has missed his last daily dose, he is likely to assume that he is coming down with a cold. Continued failure to resume treatment will lead to an abstinence syndrome, milder, but more prolonged than that following heroin withdrawal. On the other hand, addicts using other opiates, most notably heroin, go through a series of daily gyrations. Typically, the heroin user wakes in the morning feeling ill, injects some heroin and becomes high or perhaps merely normal. After several hours, he again starts to feel ill, injects more heroin, gets high, comes down, takes another injection, and so forth.

Results

There are now six years of experience with methadone maintenance. There are now perhaps 10,000 patients in about 50 programs. Results have uniformly been good. In round numbers, about 80 percent of the patients who have started remain in the program and free of dependence on the use of opiates other than methadone. Of these 80 percent, most have resumed productive lives; the remainder, though unemployed, no longer engage in illicit enterprise. Our experience in a pilot project at Orange County Medical Center confirms this result.

It is of importance to note that some programs have experimented with daily doses of methadone substantially below the level required for "narcotic blockade" and even below that required for suppression of "drug hunger."[10,11] These programs report more heroin use and higher failure rates than do those which use higher maintenance levels.

The 20 percent who must be removed from standard programs fail either because they abuse non-opiate drugs, particularly alcohol, choose to discontinue, usually in order to move elsewhere, or though freed from the costs of daily heroin use, persist in criminal activities, while a few may be so disruptive that their behavior cannot be tolerated.

The early reports of this success seemed incredible and even observers who did not doubt the accuracy of the data assumed that it was a result of such factors as the selection of patients or the charisma of the therapist.[12] Thus, the first reports in 1965 of the usefulness of methadone maintenance were met with a range of responses, from enthusiasm through skepticism to outrage. It had, after all, been American Medical Association policy since 1924 that maintenance of addicts, with rare exceptions, was improper. This policy had been so thoroughly accepted that few physicians recognized that there had ever been any debate at all. What most American physicians did not know, and perhaps still do not know, was that the original decision to discontinue maintenance techniques for addicts was the subject of prolonged and bitter debate between 1915 and 1924. Those who supported the physicians' prerogative to prescribe and the addicts' prerogative to receive maintenance treatment may well have surrendered in 1924 because Treasury Department regulations already precluded its possibility. Over the next 40 years, those few physicians, sociologists and lawyers who suggested re-examination of the maintenance technique were met with blistering reproach. Few physicians have recognized that the maintenance approach, which to this day is referred to in AMA policy as "generally inadequate and medically unsound" had never been adequately tested and that the rejection of this medical technique was based on argument rather than on evidence.[13]

Thus, the skeptical and even hostile reception methadone maintenance received in 1965 can be easily understood. During the next two or three years, the results remained so persistently and startlingly good that skepticism turned to support and even some of the bitterest critics modified their tones. The turning point can be marked by the publication of the progress report of the Methadone Maintenance Evaluation Committee published in December, 1968.[14] This select, and independent committee, unanimously expressed the conviction that the results were "most encouraging" and recommended continued intake of new patients as rapidly as facilities would allow, as well as expansion of the program to other units.

More recently, the *Medical Letter on Drugs and Therapeutics* reported:

> "Methadone therapy now offers substantial hope of rehabilitation for heroin and other opiate addicts. Despite the fact that it substitutes one addiction for another, Medical Letter editors and consultants are convinced that no other presently available therapy offers comparable promise for the many thousands of heroin addicts who are seeking help. Legally, methadone therapy is still experimental in the United States; practically, its effectiveness has been adequately established and its benefits clearly outweigh its hazards."[7]

And lastly, Federal guidelines for methadone maintenance programs have been published.[8]

The Use of Methadone in Maintenance Therapy

The medical aspects of the management of patients are relatively simple. Methadone is an easy drug to work with. Missing one day's medication or taking a double dose carries no risk to the patient and, at most, may produce some discomfort. Great caution, however, is necessary to prevent accidental ingestion by non-tolerant persons, especially children.

The problems of methadone maintenance are not medical but administrative. Because of concern over the possibility of diversion of the drug, patients must during the early phases of treatment, report each day to take their medication under supervision. As the patient becomes better known to the doctor and staff and his reliability is established, he may be given alternate doses to take home for self-administration. Regular urinalysis is performed to determine drug use and supervised ingestion is used to make certain that the patient's tolerance remains established.

Because the majority of patients either work or go to school, facilities must be open at reasonably convenient times. Physicians and nurses must be employed to evaluate ongoing treatment and to dispense medication; regular urinalysis must be done; medications must be properly prepared; new patients must be properly evaluated; and all patients should receive such ancillary care as they may need. Careful and extensive record-keeping is necessary. It is these administrative problems which consume most staff time in methadone maintenance programs.

Some Commonly Asked Questions

A number of questions are repeatedly asked by those unfamiliar with methadone maintenance.

- *Aren't patients who receive 100 or 150 mg of methadone per day either high or sedated or both? Aren't they like "zombies"?*

No. Because of the tolerance which develops, the patients feel normal; they are physically and mentally active and alert and their thinking and coordination is not impaired. In no way is the rubric "zombie" justified.

- *Methadone maintenance doesn't cure addiction; isn't it merely a crutch?*

Methadone maintenance is not a cure in the sense that the disease process has been eliminated; but there are many examples of non-curative but currently indispensable prosthetic maneuvers in medicine. We fit patients with artificial limbs, eyeglasses and hearing aids; we have little hesitancy in prolonged prescription of digitalis for a failing heart, diphenylhydantoin for an epileptic or chlorpromazine for a schizophrenic patient. These treatments also do not "cure." Even that ancient and useful device, the crutch, is not debased by calling it "*merely* a crutch" when it permits a person to ambulate who otherwise could not do so.

- *Since addiction is presumably a symptom of an underlying psychiatric disorder, doesn't methadone maintenance just treat the symptoms and not solve the basic problem?*

Despite years of study, efforts to find the so-called underlying disorder have yielded little which has been useful in treatment. Though some programs have claimed great success, they have had only limited appeal and though they have helped some addicts, regrettably they have had little impact on the over-all problem.

- *Are you not merely switching from one addiction to another, from an illegal addiction to a legal one?*

Though the patients are dependent on methadone instead of heroin, the differences are far greater than merely the question of switching addictions or of legality. Pharmacologically methadone is substantially different from heroin or other opiates. Persons dependent on heroin and most other opiates swing several times a day between being high and being sick, a phenomenon which does not occur at all with methadone maintenance. Heroin users inject the drug into

themselves with little concern for sterility, with drugs of unknown dosage and unknown constituents. Methadone patients take a single daily oral dose. Clearly, the differences between methadone patients and those using other opiates goes far beyond the question of whether a dependence exists or of legality and into gross differences in pharmacology and the vast differences between being a methadone patient or a street addict.

• *Is it not immoral to maintain an addiction?*

The technical fact that dependence is produced is immaterial once it is determined that prolonged therapy is necessary. Since patients are under medical supervision, withdrawal from methadone can be accomplished if it is indicated, by the usual means of gradual dose decrease. The only immorality, as I view it, would be to deprive a proper candidate who requests it from receiving it.

• *Since the majority of addicts are rather antisocial individuals anyway, what good will it be for them?*

Despite a criminal or antisocial background, the majority of addicts placed on methadone maintenance desist from these forms of behavior. This has been one of the most surprising and gratifying results of these programs.

• *What proportion of addicts will volunteer for methadone?*

Nobody has yet run out of volunteers. From my personal experience, I would guess that a majority of addicts will willingly enter methadone maintenance programs when they become available. The problem at the moment and for the near future is not whether there will be enough addicts for the programs, but whether there will be enough programs for the addicts.

• *How long must the patient continue to receive methadone?*

This is not known. It is possible that many, if not all, may require this treatment indefinitely. Further studies will be needed to determine this. The extended nature of the treatment is its major disadvantage. Neither patient nor physician is happy about the prospects of long-term treatment. This has nothing to do with the propriety of the treatment, rather with the limitations imposed on any chronic patient.

• *As the patient develops tolerance for methadone, won't he need more and more?*

Though minor adjustments of the maintenance dose might be necessary, as often toward a decrease, maintenance levels are stable.

• *Who should be excluded from methadone maintenance?*

Addicts without a substantial or substantiated history of physical dependence on opiates should not be accepted, nor should those who, though deeply involved in drug use, have had only moderate contact with opiates.

• *Doesn't the establishment of methadone maintenance programs really mean that we are giving up on solving the problem of addiction?*

This is not surrender at all. It provides hope where now there is mostly despair and prison. Though we still have an obligation to learn more of the nature of the problem and seek better solutions, we also have an obligation to those who are currently ensnared in the addict life.

Methadone maintenance is not perfect nor is it ideal, it is merely the most widely applicable and useful measure that we now have to control the problem.

• *What effect will methadone maintenance programs have on the long-term problem of heroin addiction?*

Heroin addiction, almost universally, is a process passed on from a user to a non-user. Most street level heroin dealers are in the business to support their own addiction. An addict who has dealt in heroin who is now on methadone no longer deals in heroin. Nor, parenthetically, is there any evidence that there has been any more than trivial diversion of methadone from well-run maintenance programs. Methadone maintenance, if widely applied, promises to be a most effective way of reducing new heroin addiction.

Conclusion

Though questions have been raised regarding the moral, ethical and medical considerations of methadone maintenance, most of these objections are groundless, while the remainder are trivial.

The cost of the treatment is moderate, perhaps $1,000 to $2,000 for the first year and $500 to $1,000 a year thereafter. Though part of the cost of treatment may be met by patients through fees, some public funding is essential. The potential savings to the community of the costs of addict caused crime, as well as the costs of law enforcement and incarceration are vast. The value of the salvage of tens of thousands of lives, the restoration of addicts to their communities, their families and themselves, cannot be measured.

Methadone maintenance is not a panacea. Some

opiate-dependent persons will not accept it because they prefer to make an effort at abstinence. Others are not interested because they prefer the perils and pleasures of heroin. Some who request methadone maintenance may prove to be unsuitable for it or may fail in the program because they persist in misusing other drugs or misbehaving in other ways. But a treatment which offers so much hope to so many patients suffering from so serious a disorder must as promptly as possible be made available to all addicts who can benefit from it. Though further research to improve the therapy and extend our knowledge is necessary (and what therapy is there that cannot be further improved?) we have in methadone maintenance a safe and effective treatment. Were the disability of heroin addiction a minor one, there might be justification to the view that we must proceed very slowly. But addiction is so serious that unnecessary delay may be disastrous to many.

This is the time for responsible but bold action to establish a large number of carefully run programs throughout the state.

REFERENCES

1. Narcotic Use History: Felon Population in Prison and on Parole as of December 31, 1966. Department of Corrections, March 24, 1967
2. Summary Statistics, Civil Commitment Program for Narcotic Addicts, 1961-1966. Department of Corrections, December 31, 1966, p 5
3. Kramer JC: New directions in the management of opiate dependence. New Physician 18:203-209, 1969
4. Dole VP, Nyswander ME, Warner A: Successful treatment of 750 criminal addicts. JAMA 206:2708-2711, 1968
5. Ausubel DE: The Dole-Nyswander treatment of heroin addiction. JAMA 195:949-950, 1966
6. Dole VP, Nyswander ME: Rehabilitation of heroin addicts after blockade with methadone. New York J Med 66:2011-2017, 1966
7. Medical Letter on Drugs and Therapeutics 11:97-99, 1969
8. Food and Drug Administration: Fed Register 35:9014-9015, June 11, 1970
9. Fink M, Zaks A, Roubicek J, et al: Methadone induced cross tolerance to heroin. Personal communication.
10. Weiland WF: Personal communication
11. Paulus I, Halliday R: Rehabilitation and the narcotic addict: Results of a compartive methadone withdrawal program. Canad Med Assoc J 96:655-659, 1967
12. Vaillant CE: Methadone—another view (letter). Hospital Practice 2:12, 1967
13. Lindesmith AR: Addiction and the law, chap 1, The Addict and the Law. Bloomington, Indiana University Press, 1967
14. Progress report of evaluation of methadone maintenance treatment program as of March 31, 1968. JAMA 206:2712-2714, 1968